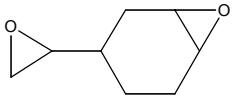
4-VINYL-1-CYCLOHEXENE DIEPOXIDE
CAS No. 106-87-6
First listed in the *Seventh Annual Report on Carcinogens*



CARCINOGENICITY

4-Vinyl-1-cyclohexene diepoxide is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. Carcinogenesis and toxicology studies were conducted on rats and mice by administering the chemical (97% pure) in acetone by dermal application for varying lengths of time. It was determined that 4-vinyl-1-cyclohexene diepoxide was carcinogenic to skin at the site of application in both male and female rats and mice. Although the neoplasms were diagnosed according to the predominant cell type present, all were considered to originate primarily from the basal cells of the skin and adnexal structures, showing different degrees of differentiation to basal, squamous, or sebaceous. In both rats and mice, the predominant skin neoplasms seen were squamous cell carcinomas. However, basal cell adenomas and/or carcinomas were observed more frequently in rats (14 animals) than in mice (1 animal). The current studies show that the predominant type of skin neoplasm related to chemical exposure is squamous cell carcinoma. The apparent latent period for development of these neoplasms was longer for rats than for mice and shorter at higher doses than at lower doses. In a study conducted with mid- and high-dose female mice, benign and malignant neoplasms of the ovary occurred. A few of these neoplasms that were malignant, metastasized to the lungs. Two of the nine animals in the high-dose group and one animal in the mid-dose group had granulosa cell tumors of the ovary. At the end of the study, the incidences of these neoplasms were similar in mid- and high-dose groups. There was a morphological continuum from tubular hyperplasia to benign mixed tumors in mice. No such neoplasms were observed in female rats. The occurrence of these neoplasms is uncommon in rodent chemical carcinogenicity studies (NTP 362, 1989).

No studies on the potential carcinogenicity of 4-vinyl-1-cyclohexene diepoxide in humans were identified. However, NIOSH has listed it as a suspected occupational carcinogen. The major manufacturer of the chemical has also labeled it as carcinogenic in mice when applied to skin and has warned users to avoid skin contact and exposure to vapors (NTP 362, 1989).

PROPERTIES

4-Vinyl-1-cyclohexene diepoxide is a colorless, odorless liquid. It is soluble in water and has an open-cup flash point of 110 degrees C. It reacts with active hydrogen compounds (such as alcohols and amines). It is slowly hydrolyzed in water.

USE

4-Vinyl-1-cyclohexene diepoxide is used as a reactive diluent for other diepoxides and for epoxy resins derived from bisphenol A and epichlorohydrin. It has been proposed for use as a chemical intermediate (i.e., in condensation reactions with dicarboxylic acids), a monomer for preparation of polyglycols containing epoxy groups, and for homopolymerization to a three-

dimensional resin. In addition, this chemical is used as a monomer in the production of epoxy resins for coatings and adhesives (NTP 362, 1989).

PRODUCTION

Chem Sources identified one supplier of analytical grade 4-vinyl-1-cyclohexene diepoxide among the four listed in 1990 (Chem Sources, 1991). One company has been identified as the major manufacturer of 4-vinyl-1-cyclohexene diepoxide in the United States (NTP 362, 1989). The 1977 TSCA inventory reported on manufacturer and one importer in 1977, production volumes for both the producer and the importer are confidential.

EXPOSURE

The primary route of potential occupational exposure is by inhalation or dermal contact. The National Occupational Exposure Survey (NOES), conducted by NIOSH between 1981 and 1983, estimated that 1,997 workers in the United States were potentially exposed to 4-vinyl-1-cyclohexene diepoxide. A threshold limit value/time-weighted average of 10 ppm (60 mg/m^3) for skin has been recommended by the American Conference of Governmental Industrial Hygienists (NTP 362, 1989). Animal studies show that this chemical can cause irritation to the eyes and skin of rabbits. It also can cause acute respiratory tract irritation and congestion of the lungs. This chemical has been associated with testicular atrophy, leucopenia, and necrosis of the thymus (Sittig, 1985).

The National Toxicology Program (NTP) has studied the fate of a single dermal application of radiolabeled 4-vinyl-1-cyclohexene diepoxide in female rats and mice. These studies were conducted to determine if there were differences in disposition which could explain the differences in toxicity observed in rats and mice. The results indicated that 30% of the dose applied to the skin is absorbed over a 24-hour period for both rats and mice, and only 1-3% of the dose remained on the skin. By 24 hours, 70-80% of the absorbed dose had been eliminated from the body, virtually all in the urine. When rabbits were exposed to the chemical dermally, it caused edema and redness comparable to a mild to first-degree burn. The dermal application of the chemical is more toxic than any other route of exposure in rabbits, and the dermal LD_{50} in rabbits is reported to be 0.62 ml/kg body weight. The oral LD_{50} for rats is 2,130 mg/kg, and the inhalation LC_{50} is 800 ppm for 4 hours. 4-Vinyl-1-cyclohexene diepoxide is a mild to moderate skin irritant in humans; when tested in guinea pigs, skin sensitization occurred infrequently (NTP 362, 1989).

REGULATION

EPA regulates 4-vinylcyclohexene (4-VCH), a site-limited intermediate in the production of 4-vinylcyclohexene diepoxide, under the TSCA. EPA has signed an enforceable Testing Consent Order for 4-VCH with nine manufacturers, who have agreed to perform subchronic effects mutagenicity, pharmacokinetics, and aqueous volatilization rate test on 4-VCH. OSHA final rule regulates the 8-hr time-weighted average (TWA) of 4-vinyl-1-cyclohexene diepoxide to 10 ppm. OSHA regulates 4-vinyl-1-cyclohexene diepoxide under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-150.